Patent
Attorney's Docket No. 033025-002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
	)	
Naohiro TAKEMOTO et al.	)	Group Art Unit: Unassigned
	)	
Application No.: 10/009,566	)	Examiner: Unassigned
	)	
Filed: December 12, 2001	)	
	)	
For: AMINOPHENOXYACETAMIDE DERIVATIVES AND PHARMACEUTICAL COMPOSITION CONTAINING THEREOF	)	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In complete response to the Notification of Missing Requirements Under 35 U.S.C. § 371 mailed on February 27, 2002, please amend the above-identified application as follows:

IN THE SPECIFICATION:

In compliance with 37 C.F.R. § 1.823(a), please insert the attached paper copy of the Sequence Listing after the last page of the specification of the above-identified application to replace the Sequence Listing filed on December 12, 2001.

REMARKS

Entry of the foregoing and prompt and favorable consideration of the subject application are respectfully requested.

By the foregoing amendment, the specification has been amended to insert the attached paper copy of the Sequence Listing after the last page of the specification to replace the Sequence Listing filed on December 12, 2001.

In the event that there are any questions relating to this amendment, or the application in general, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
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(703) 836-6620

Date: April 29, 2002

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Naohiro TAKEMOTO et al	)	Group Art Unit: To be assigned
	)	
Application No.: To be assigned	)	Examiner: To be assigned
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PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination of the above-identified application, applicants respectfully request entry of the following amendments:

In The Specification:

Please insert, after page 58 of the specification, the Abstract of the Invention, attached hereto.

Please replace the paragraph beginning at page 3, line 13, with the following:

--On the other hand, the lower molecular weight compounds capable of inducing the production of CalbindinD-28k protein can be easily prepared into the various kinds of pharmaceutical compositions by the conventional technique. Therefore, these lower molecular weight compounds would induce the production of the neuroprotective

CalbindinD-28k protein once easily administered into a body, showing the buffering action against the increase of the intracellular Ca^{2+} concentration. That is, these lower molecular weight compounds can be effective pharmaceutical compounds for improving and treating cerebral functional and organic disorders.--

In The Claims:

Please cancel claims 4-21, without prejudice or disclaimer to the subject matter disclosed therein.

Please add the following new claims:

--22. A composition comprising an aminophenoxyacetamide derivative or a pharmaceutically acceptable salt thereof represented by the formula (I) in claim 1 as an active ingredient.--

--23. A composition comprising an aminophenoxyacetamide derivative or a pharmaceutically acceptable salt thereof represented by the formula (I) in claim 2 as an active ingredient.--

--24. A composition comprising an aminophenoxyacetamide derivative or a pharmaceutically acceptable salt thereof represented by the formula (I) in claim 3 as an active ingredient.--

--25. A method for inducing the production of CalbindinD-28K wherein said method comprises administering to a patient a composition according to claim 22.--

--26. A method for inducing the production of CalbindinD-28K wherein said method comprises administering to a patient a composition according to claim 23.--

--27. A method for inducing the production of CalbindinD-28K wherein said method comprises administering to a patient a composition according to claim 24.--

--28. A method for improving or treating cerebral function and/or organic function disorders wherein said method comprises administering to a patient a composition according to claim 22.--

--29. The method of claim 28, wherein said cerebral function disorders are caused by ischemic disorders.--

--30. The method of claim 29, wherein said ischemic disorders are selected from the group consisting of cerebral infarction, intracerebral hemorrhage and cerebral arteriosclerosis.--

--31. The method of claim 28, wherein said organic function disorders are selcted from the group consisting of senile dementia, cerebral injury, cerebral operation, Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis.--

--32. A method for improving or treating cerebral function and/or organic function disorders wherein said method comprises administering to a patient a composition according to claim 23.--

--33. The method of claim 32, wherein said cerebral function disorders are caused by ischemic disorders.--

--34. The method of claim 33, wherein said ischemic disorders are selected from the group consisting of cerebral infarction, intracerebral hemorrhage and cerebral arteriosclerosis.--

--35. The method of claim 32, wherein said organic function disorders are selcted from the group consisting of senile dementia, cerebral injury, cerebral operation, Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis.--

--36. A method for improving or treating cerebral function and/or organic function disorders wherein said method comprises administering to a patient a composition according to claim 24.--

--37. The method of claim 36, wherein said cerebral function disorders are caused by ischemic disorders.--

--38. The method of claim 37, wherein said ischemic disorders are selected from the group consisting of cerebral infarction, intracerebral hemorrhage and cerebral arteriosclerosis.--

--39. The method of claim 36, wherein said organic function disorders are selcted from the group consisting of senile dementia, cerebral injury, cerebral operation, Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis.--

--40. A method for selecting a neuroprotective compound, wherein said method comprises evaluating the activation of receptors for various kinds of physiologically active substances and the phosphorylation of the FGF receptor caused by the induction of CalbindinD-28k production.--

--41. The method for selecting a neuroprotective compound according to claim 40, wherein said method comprises evaluating the autophosphorylation of the FGF receptor.--

--42. The method for selecting a neuroprotective compound according to claim 40, wherein said method is performed by evaluating for neuroprotective effect of the

physiologically active substance against glutamate-induced neurodegeneration together with one or more of the following tests (i)-(iii):

(i) evaluating for antagonism against the neuroprotective effect of the physiologically active substance by treatment with MTA (5-deoxy-5-methyl-thioadenosine), which inhibits autophosphorylation of the FGF receptor, and by treatment with inhibitors of various physiologically active substance receptors, to determine if the neuroprotective effect is due to autophosphorylation of receptors of the FGF receptor;

(ii) evaluating the CalbindinD-28k inducing effect of the physiologically active substance; or

(iv) confirming that the neuroprotective effect of the physiologically active substance is due to its inducing CalbindinD-28k production, by treating with the antisense oligonucleotide of CalbindinD-28k and determining if CalbindinD-28k production is antagonized.--

--43. The method according to claim 18, wherein said physiological active substance receptors are selected from the group consisting of receptors for neurotrophin-3 (NT-3), neurotrophin-4/5 (NT-4/5), brain-derived neurotrophic factor (BDNF), insulin-like growth factor-I/II (IGF-I/II), platelet-derived growth factor (PDGF), and estrogen.--

--44. A neuroprotective compound selected by the method according to claim 40.--

--45. A composition comprising a neuroprotective compound according to claim 44.--

--46. A method of treating or improving cerebral functional disorders and/or cerebral organic disorders, wherein said method comprises administering the composition according to claim 45 to a patient in need thereof.--

--47. The method according to claim 46, wherein said cerebral functional disorders are caused by ischemic disorders.--

--48. The method according to claim 47, wherein said ischemic disorders are selected from the group consisting of cerebral infarction, intracerebral hemorrhage and cerebral arteriosclerosis.--

--49. The method according to claim 46, wherein said cerebral organic disorders are selected from the group consisting of senile dementia, cerebral injury, cerebral operation, Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis.--

REMARKS

Entry of the foregoing and favorable consideration of the subject application, in light of the following remarks, are respectfully requested.

By the present amendment, the claims have been amended to place them in the proper format for examination. Each of the added claims corresponds to a claim in the International application. No new matter has been added by the present amendment.

In the event that there are any questions relating to this Preliminary Amendment, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Dawn M. Gardner
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Date: December 12, 2001

Attachment to Preliminary Amendment dated December 13, 2001

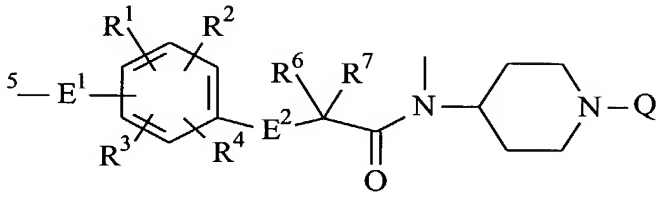
Marked-up Copy

Page 3, Paragraph Beginning at Line 13

--On the other hand, the lower molecular weight compounds capable of [including] inducing the production of CalbindinD-28k protein can be easily prepared into the various kinds of pharmaceutical compositions by the conventional technique. Therefore, these lower molecular weight compounds would induce the production of the neuroprotective CalbindinD-28k protein once easily administered into a body, showing the buffering action against the increase of the intracellular Ca^{2+} concentration. That is, these lower molecular weight compounds can be effective pharmaceutical compounds for improving and treating cerebral functional and organic disorders.--

ABSTRACT OF THE INVENTION

The present invention relates to an aminophenoxyacetamide derivative of the formula (I):



(I)

wherein R^1 to R^4 are, independent from each other, a hydrogen atom or an optionally substituted alkyl group; E^1 is $-NR^4-$; and E^2 is an oxygen atom or $-NR^{10}-$; Q is the group -X-Y-Q', wherein X and Y are connecting bonds or X is an alkylene or alkenylene group and Y is selected from a group comprising C=O, NHC(=O), and C(=O)NH, and Q' is a hydrogen atom or a phenyl or pyridyl group which may be substituted; and pharmaceutically acceptable salts thereof. The present invention further relates to compositions comprising compounds of the formula (I) and methods of using said compounds for treating cerebral functional disorders and cerebral organic disorders.